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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,703	08/19/2003	Louis A. Pena	30817-1008-CIP	7990

5179 7590 10/17/2006

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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,703	PENA ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *1-7, 21-26, 46-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-20 and 27-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 8-20 and 27-45 with a species of synthetic HBGF analog (F2A4) in the communication filed on 08/17/2006 is acknowledged.

The traversal with respect to Groups II, V, VI, VII and VIII is on the ground that there is no undue burden to search Groups II, V, VI, VII, and VIII. Applicants allege that each and every one of the groups is shown as classified in the same class (514) and the same subclass (12+).

Given that each of the inventions is asserted to be in the same class and subclass, it is submitted that the second criteria under MPEP § 803 is not met, and that no serious burden is demonstrated requiring restriction.

This is not found persuasive for the following reasons:

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(c-I), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof: (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, the separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

Applicant argues that no burden is placed on the examiner to consider all claims. As discussed above, the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner. Furthermore, each group requires a non-coextensive sequence and non-patent literature search.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-7 and 21-26, and 46-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Claims 8-20 and 27-45 are pending and under examination.

Claim Objections

Claim 29 is objected to because of the following informalities: claim 29 contains nonelected subject matter. Appropriate correction is required.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/224,268 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The claimed invention drawn to a heparin-binding growth factor (HBGF) analog of formula II. The heparin-binding growth factor (HBGF) analog of formula II in the U.S. application 10/224,268 has a different formula II from the one disclosed in the instant application: U.S. application 10/644,703 filed on 08/19/2003. Therefore, the instant application is given the priority of the U.S. application 10/644,268 filing date of 08/19/2003.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 8-20 and 27-45 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 10/224,268. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112 (Written Description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-20 and 27-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 8 is drawn to a heparin-binding growth factor (HBGF) analog; claim 8 is thus genus claims. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the

polypeptide and does not clearly defined analogs for any of the heparin-binding growth factor. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish sequences in the genus from for any analog of the heparin-binding growth factor (HBGF) are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a heparin-binding growth factor (HBGF) analog of formula II is insufficient to describe the genus.

The written description requirement for a claimed genus' may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus any analog of heparin-binding growth factor (HBGF).

There is no description of the conserved regions, which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to

enable one of skill to isolate and identify the polypeptides encompassed by the limitations. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 8-20 and 27-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthetic HBGF analog of Formula II (species F2A4), does not reasonably provide enablement for variants of the synthetic HBGF analog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

Breath of the claims and working examples

The claims are drawn to the synthetic HBGF analog species F2A4. The breadth of Claims 8-20 and 27-45 is too large since the specification fails to provide any guidance on how to produce other compounds of Formula II that retain the function of F2A4. In other words, no discussion or working examples, in the instant case, as to what amino acids and linking

molecules are necessary to maintain the functional characteristics of the claimed compounds are disclosed. F2A4, for example, has been shown in the instant Specification to function quite unlike full-length FGF2 as well as unlike the other two growth factor analogs based on Formula I or Formula II (see Figure 6 and figure 10).

Unpredictability and state of the art

Although the disclosed compounds share several common structural features, relevant art (see below) shows that members of a class having structural homologies in common do not always share specific and substantial functional attributes or utilities. This was shown in the instant disclosure (compare the activities of FGF, F2A3 and F2A4), as well as in recent literature in which heparin- binding domains of growth factors have been manipulated or mutated (Yoneda, et al, 2000, Nature Biotech., 18: 641-644; Verrecchio, et al, 2000, J. Biol. Chem., 275(11): 7701-7707) resulting in functionally-different compounds. These examples and others illustrate that it is not predictable as to which amino acids and analogs are necessary to maintain the functional characteristics of a synthetic peptide analog.

The amount of direction or guidance present

The specification does not reasonably provide enablement for use of variants of HBGF analog F2A4. Claims 1-7, 9-20, 22-24, 32-37 and 43-45 encompass numerous defined and undefined variants of the analog without precise recitations of structure and function and without data that would enable the entire encompassed genus (i.e., that would show them as functionally identical). Claims 1-7, 9-20, 22-24, 32-37 and 43-45 are directed to synthetic analogs of growth factors, each variant comprising a heparin binding domain attached with variable linker molecules to a monomer or dimer fragment of a growth factor. Dependent claims

specify the amino acids and spacer molecules presumably encompassed by Formula I (see, for example, Figure 2).

Neither the Specification nor the current literature is enabling for the full scope of the claimed compounds, with the assurance that enabled compounds that are functionally equivalent to F2A4 can be made without undue experimentation and with the assurance that they would have the desired properties of the F2A4 analog. Furthermore, since the claims only require that the compound bind to heparin- a probable characteristic of nearly every peptidic compound- the claims embrace variants that may be inactive at a growth-factor receptor. The specification does not disclose how to use such inactive variants.

The quantity of experimentation needed

Due to the large quantity of experimentation necessary to determine an activity or property of the claimed HBGF compounds such that it can be determined how to use the claimed compounds and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex the breadth of the claims which fail to recite particular biological activities--undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

In summary, the specification does not provide a description of a repeatable process of producing, nor of working examples of making the HBGF compounds that are functionally equivalent to F2A4. In addition, the predictability of the art is low with regards to the knowledge of what effects altering F2A4 would have on the functionality of the compound. For this reason, undue experimentation would be required to determine a structure-function relationship for each possible polypeptide encompassed by the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-20 and 27-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites an HBGF chain comprising a number of "atoms." However, one skilled in the art cannot determine the metes and bounds of the claimed invention because one does not normally count the atoms (e.g., C, H, O, N) in a polypeptide chain, but rather amino acids. Amending claims to recite "amino acids" or "residues," for example would be remedial.

Conclusion

No claims are allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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October 11, 2006

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